

- IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

The amino acid sequence encoding PRO347 is shown in Figure 3 of the '702 application, which corresponds with SEQ ID NO:50 in the '664 application.

4. The attached sequence listing is a true and correct copy of the amino acid sequence of PRO347, as set forth in the '702 application.

5. Upon isolating and sequencing DNA44176, which encodes the PRO347 polypeptide, I appreciated that the invention of DNA44176 included variant sequences, such as allelic variant sequences, variant sequences that arise due to the degeneracy of the genetic code, and variant sequences that arise naturally or synthetically due to additions, deletions or substitutions of nucleic acids.

6. For example, in the '702 application we defined "native sequence PRO347 polypeptide" at page 4 as specifically encompassing:

naturally-occurring truncated or secreted forms of a PRO347 polypeptide (e.g., an extracellular domain sequence), naturally-occurring variant forms (e.g., alternatively spliced forms) and naturally-occurring allelic variants of a PRO347 polypeptide.

7. Also, in the '702 application, we noted, at page 7:

In addition to the full-length native sequence PRO347 polypeptide described herein, it is contemplated that PRO347 variants can be prepared. PRO347 variants can be prepared by introducing appropriate nucleotide changes into the PRO347-encoding DNA, or by synthesis of the desired PRO347 polypeptide.

8. As one of skill in the art, I appreciated at the time DNA44176 was sequenced, that variations could be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis.

Techniques for achieving sequence variation using site-directed mutagenesis are described in Carter *et al.*, *Nucleic Acids Res.*, 13:4431 (1985) (attached hereto as Exhibit A) and Zoller *et al.*, *Nucleic Acids Res.*, 10:6487 (1982) (attached hereto as Exhibit B). Techniques for achieving sequence variation using cassette mutagenesis are described in Wells *et al.*, *Gene* 34:315 (1985) (attached hereto as Exhibit C).

These techniques were described in the '702 application at page 8.

9. Prior to July 15, 1999, the filing date of WO 99/35170, I conceived and reduced to practice in the United States the nucleic and amino acid sequences encoding PRO347, as demonstrated by their disclosure in U.S. Provisional Application Serial No. 60/113,296 ("the '296 application"), filed 12/22/98. The nucleic acid sequence encoding PRO347 is identified as DNA44176 and is shown in Figure 13 (SEQ ID NO:13) of the '296 application. This sequence corresponds to SEQ ID NO:49 in the '664 application. The amino acid sequence encoding PRO347 is shown in Figure 14 (SEQ ID NO:14) of the '296 application, which corresponds with SEQ ID NO:50 in the '664 application.

10. The attached sequence listing is a true and correct copy of the amino acid sequence of PRO347, as set forth in SEQ ID NO: 14 (Figure 14) of the '296 application.

11. I declare that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above applications or any patent granted therein.

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Paul Godowski, Ph.D.

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Date